

**DATA EVALUATION RECORD
CHRONIC (REPEATED DOSE) TOXICITY TEST WITH THE HONEY BEE
NON-GUIDELINE**

1. **CHEMICAL:** Spiromesifen-enol **PC Code:** 024875

2. **TEST MATERIAL:** Spiromesifen-enol **Purity:** 99.0%

3. **CITATION**

Authors: Tomé, H.V.V. and Porch, J. R.
Title: Spiromesifen enol: Effects of a Repeated (Chronic)
Exposure on Honey Bee (*Apis mellifera*) Larvae in an
in vitro Laboratory Testing Design
Study Completion Date: April 23, 2019
Laboratory: EAG, Inc.
Sponsor: Bayer Crop Science LP
Study No.: 149H-109
MRID: 50862201
DP Barcode: 452560

4. **REVIEWED BY:** Julie Burns, Environmental Scientist, CDM/CSS-Dynamac JV

Julie Burns
Signature: **Date:** 7/16/2019

APPROVED BY: Moncie V. Wright, Ph.D., Environmental Scientist, CDM/CSS-Dynamac JV

Moncie V Wright
Signature: **Date:** 7/22/2019
(Stats re-do & DER update completed 10/21/2019)

5. **REVIEWED BY:** Susan Thomas, Biologist, ERB IV, Environmental Fate and Effects Division, USEPA

Signature: **SUSAN THOMAS** Digitally signed by SUSAN THOMAS
Date: 2020.01.28 12:54:17 -05'00' **Date:** 01/28/2020

APPROVED BY: Cameron Douglass, PhD., Biologist, ERB IV, Environmental Fate and Effects Division, USEPA

Signature: *Cameron Douglass* **2020.01.28 12:31:07** **-05'00'** **Date:** 01/28/2020

This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel. The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies.

6. STUDY PARAMETERS:

Test Species: Honey bees, (*Apis mellifera* L.)
Age of Test Organisms at Test Initiation: Approximately first instar larvae
Exposure Duration: 20 days

7. CONCLUSIONS:

Individual synchronized honey bee (*Apis mellifera*) larvae (~1st instar) were exposed *in vitro* to spiromesifen enol (99.0%) on Days 3 through Day 6 of the study at the nominal and measured diet concentrations and daily doses reported in the table below. Daily doses were calculated by dividing the study author-reported nominal and measured cumulative doses by the number of days of exposure (4). The mean measured dietary concentrations and measured cumulative doses were calculated by the study author based on the average concentration of the analyzed Diet B and Diet C samples, adjusted for purity.

Nominal Diet Concentration (mg a.i./kg diet)	Mean-Measured Diet Concentration (mg a.i./kg diet)	Nominal Daily Dose (µg a.i./larva/day)	Measured Daily Dose (µg a.i./larva/day)
0.8	0.66	0.03	0.03
1.6	1.3	0.08	0.06
3.1	2.6	0.13	0.12
6.3	5.8	0.25	0.24
13	12	0.50	0.50
25	21	1.00	0.80

Dimethoate was tested as a reference toxicant at a nominal dose of 7.39 µg a.i./larva (46.3 mg a.i./kg). In this study, a replicate was defined as each individual larvae. All groups consisted of 36 larvae per treatment group, placed within 48-well cell culture plates.

All endpoints were significantly affected by the test material in this experiment, but adult emergence was the most sensitive of the endpoints. There was a significant reduction (37-100%) in emergence in the four highest test levels, resulting in NOAEC and EC₅₀ values of 1.3 and 2.4 mg a.i./kg diet, respectively (corresponding to a NOAEL and ED₅₀ of 0.058 and 0.11 µg a.i./larva/day, respectively).

The study is **scientifically sound** and is consistent with the OECD Guidance Document for

measuring chronic (repeat dose) toxicity to honey bee larvae with a few exceptions (see guideline deviations below). The study is classified as **$\mu\text{g ai/larva/day}$** but may be used quantitatively for risk assessment purposes.

	Mortality (Day 8)	Mortality (Day 15)	Adult Emergence (Day 22)
Diet Concentration mg a.i./kg diet	LC ₅₀ : 3.3 95% CI: 2.2 - 4.8 Slope: 3.8 (2.0 - 5.6) NOAEC: 1.3 LOAEC: 2.6	LC ₅₀ : 3.25 95% CI: 2.82-3.73 Slope: N/A NOAEC: 2.6 LOAEC: 5.8	EC ₅₀ : 2.4 95% CI: 1.8 - 3.2 Slope: 3.0 (2.0 - 4.1) NOAEC: 1.3 LOAEC: 2.6
Dietary Dose μg a.i./larva/day	LD ₅₀ : 0.14 95% CI: 0.094 - 0.21 Slope: 3.9 (1.8-6.0) NOAEL: 0.058 LOAEL: 0.12	LD ₅₀ : 0.14 95% CI: 0.13-0.16 Slope: N/A NOAEL: 0.12 LOAEL: 0.24	ED ₅₀ : 0.11 95% CI: 0.078 - 0.14 Slope: 3.1 (2.0 - 4.1) NOAEL: 0.058 LOAEL: 0.12

8. ADEQUACY OF THE STUDY:

- A. Classification:** This study is **scientifically sound** and is classified as **supplemental**, but may be used quantitatively for risk assessment purposes.
- B. Rationale:** While the study data provide a dose response and are scientifically sound, there were a number of deviations from the study design described in the guidance document.
- C. Reparability:** The deficiencies outlined below for this particular study cannot be repaired, but because overall the study was determined to be scientifically sound at this time repeating the study is not warranted (*i.e.*, no additional data is required).

9. GUIDELINE DEVIATIONS

The procedures used in this study are based on OECD Guidance Document No. 239 dated July 15, 2016 and Schmehl et al. The following deviations from OECD 239 were noted by the reviewer:

1. The % composition of Diets A and B deviated from OECD guidance.
2. The shape of the grafted larvae at transfer was not reported. OECD recommends that newly hatched larvae are selected that have not yet formed a "C" shape.
3. It was not reported if hives were kept in accordance with standard beekeeping practices. Additionally, the health of the colonies was not reported.
4. The average relative humidity during the pupal stage was reported to be 72.06%, which was lower than OECD guidance of $80\% \pm 5\%$. Minimum and maximum values were not reported.
5. The exact source of the hives was not reported.

These deviations **do not** affect the acceptability of the study.

- 10. SUBMISSION PURPOSE:** To determine the chronic effects on growth, development and survival and sublethal effects of technical grade spiromesifen-enol on the honey bee (*A. mellifera* L) larvae from chronic [repeat dose] exposure following the OECD Guidance Document.

11. MATERIALS AND METHODS:

A. Test Material:	Spiromesifen enol
Synonyms:	BSN 2060
Description:	White powder
Lot No./Batch No.:	AE 0920586 00 1B99 0001
Purity:	99.0%
CAS Number:	148476-30-6
Stability of compound under test conditions:	Analytical measurements of spiromesifen enol in the royal jelly diet demonstrated that the mean test item concentrations were recovered at rates ranging from 80% to 97% of nominal.
Storage conditions of test chemical:	+5 ± 5°C

Range finding test yes/no:

Yes, a preliminary study was conducted from September 17 to September 21, 2018. A second range finder test was conducted from September 24 to 29, 2019. Nominal concentrations were 3.0, 10, and 30 mg a.i./kg diet, with day 8 larval survival of 92, 33, and 0%, respectively.

B. Test Organisms

Guideline Criteria	Reported Information	Comments
Species	Honey bee (<i>Apis mellifera</i> L.)	Meets standard. <i>OECD recommends European honey bee (<i>Apis mellifera</i>)</i>
Age at beginning of test	~1st instar	Meets standard.

Guideline Criteria	Reported Information	Comments
		<i>OECD recommends that on Day 1 of study, first instar (L1) synchronized larvae (i.e., larvae of the same age) are taken from comb of three colonies.</i>
Source	Locally sourced larvae. Larvae were from three different colonies.	Meets standard. <i>OECD recommends larvae are collected from three different colonies.</i>
Were bees from disease-free colonies?	Larvae were selected from apparently healthy, queen-right hives that have not been exposed to pesticides or other in-hive treatments within 4 weeks of the test start.	Beekeeping practices were not described in detail, uncertain if meets standard. <i>OECD recommends that colonies used to obtain larvae should be adequately fed, healthy (i.e., as far as disease- and parasite-free), with a known history and physiological status.</i>
Were bees kept in conditions conforming to proper cultural practices?	Not reported.	Uncertain if meets standard.

C. Test System

Guideline Criteria	Reported Information	Comments
Test Chambers	Larvae were reared in polystyrene cell cups (internal diameter of 9 mm, depth of 8 mm) placed within the wells of sterile, 48-well tissue culture plates. Cell plates were covered with a lid.	Meets standard. <i>OECD recommends 48-well plate with each well containing a crystal polystyrene grafting cell.</i>
Temperature during exposure	Larval and pupal plates were held in a hermetically sealed desiccator and placed in an	Maximum and minimum temperatures were not reported.

Guideline Criteria	Reported Information	Comments
	<p>incubator. Temperature was monitored continuously.</p> <p><u>Larval stage:</u> average of 34.01°C</p> <p><u>Pupal stage:</u> average of 34.22°C</p> <p>The temperature did not drop below 23°C or go above 40°C. Deviations did not last for more than 30 minutes once every 24 hours.</p>	<p>Meets standard.</p> <p><i>OECD recommends incubator at 34 – 35°C. Deviations may occur but temperature should not be lower than 23°C or higher than 40°C; deviations not last more than 15 minutes once every 24 hrs.</i></p>
Relative humidity during exposure	<p>A dish with K₂SO₄ solution was placed in a hermetically sealed desiccator and monitored continuously during the larval stage to maintain relative humidity. Pupal plates were likewise kept in a hermetic incubator with a dish filled with NaCl solution to maintain relative humidity.</p> <p><u>Larval Stage:</u> average of 96.47%</p> <p><u>Pupal Stage:</u> average of 72.06%</p>	<p>Maximum and minimum relative humidity values were not reported.</p> <p>Meets standard.</p> <p><i>OECD recommends use of K₂SO₄ to maintain water saturated atmosphere.</i></p>

Guideline Criteria	Reported Information	Comments
Lighting	Constant darkness except during grafting, renewal of diet, and observations.	Meets standard. <i>OECD recommends that plates should be maintained in darkness.</i>

Feeding	<p>Each larva was fed for 6 days (except on Day 2) with a standardized amount of an artificial diet of 20 µL untreated Diet A on Day 1 (grafting), not fed on Day 2, 20µL of treated Diet B on Day 3, and fed 30, 40, and 50 µL of treated Diet C on days 4, 5, and 6, respectively. The diets were not heated up prior to feeding, in order to prevent test material breakdown.</p> <p><i>Calculated by the reviewer using diet components provided in the study report:</i></p> <p>Diet A: 44.25% weight of royal jelly + 55.75% weight of a water solution containing 1.61% weight of yeast extract, 9.51% weight of glucose + 9.51% weight of fructose.</p> <p>Diet B: 42.95% weight of royal jelly + 57.05% weight of a water solution containing 2.28% weight of yeast extract, 11.22% weight of glucose + 11.22% weight of fructose.</p> <p>Diet C: 50% weight of royal jelly + 50% weight of a water solution containing 4% weight of yeast extract, 18% weight of glucose + 18%</p>	<p>Diets A and C deviated from the OECD Guideline 239 recommended proportions.</p> <hr/> <p><i>OECD recommends that all larvae are fed once a day. Volume of diet is adjusted each day. Additional food should be added to the cell even if previous allocation has not been totally consumed. Presence of uneaten food at termination of test should be reported.</i></p> <p><i>OECD recommends:</i></p> <p><i>Diet A (D1): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 2% weight of yeast extract, 12% weight of glucose and 12% weight of fructose</i></p> <p><i>Diet B (D3): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 3% weight of yeast extract, 15% weight of glucose and 15% weight of fructose.</i></p> <p><i>Diet C (from D4 to D6): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 4% weight of yeast extract, 18% weight of glucose and 18% weight of fructose.</i></p>
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Guideline Criteria	Reported Information	Comments
	weight of fructose.	

D. Test Design

Guideline Criteria	Reported Information	Comments
Nominal test applications	<u>Diet Concentrations:</u> 0 (negative control) 0.8, 1.6, 3.1, 6.3, 13, and 25 mg a.i./kg diet <u>Daily Dietary Doses^a:</u> 0 (negative control) 0.03, 0.08, 0.13, 0.25, 0.50, and 1.0 µg ai/larva/day	Meets standard. <i>OECD recommends 5 treatments of increasing test concentrations. Alternatively, when a limit test is performed, a single dose of 100 µg ai/larva or the maximum achievable solubility (whichever is lower).</i>
Measured test applications	<u>Diet Concentrations:</u> <0.100 (<LOQ, control), 0.66, 1.3, 2.6, 5.8, 12, and 21 mg a.i./kg diet <u>Daily Dietary Doses^a:</u> 0.028, 0.058, 0.12, 0.24, 0.50, and 0.80 µg a.i./larva/day	The reviewer converted cumulative doses to daily doses, by dividing the cumulative doses by the number of days of exposure.
Number of bees exposed per dosage level	36 larvae per treatment level; larvae were from 3 different colonies.	Meets USEPA standard. <i>OECD recommends minimum of 12 larvae from each of 3 colonies allocated on the same plate to each</i>

		<i>treatment, i.e., minimum of 36 larvae per treatment.</i>
Other experimental design information	<p>The queen was isolated in an excluder on an empty frame for approximately 24 hours to provide synchronized aged eggs and subsequent larvae. After removing the queen, the frames with eggs were kept in the brood nest of the hive for approximately 75 hours. Larvae were then selected for grafting.</p> <p>The shape of the grafted larvae at transfer was not reported. Larvae with noticeable defects were not grafted.</p> <p>On Day 3, a 250 mg a.i./kg diet stock solution of spiromesifen enol was prepared by bringing 0.0038 g of active ingredient to a final mass of 15 g with Diet B. A primary diet solution was prepared by dilution with Diet B, and each test concentration was made with serial dilutions. Diets A and B were prepared fresh on the day of exposure. Diet C was prepared on Day 4 with the same methodology as the Diet B preparation. Unused Diet C was refrigerated between feeding intervals and brought to room temperature before application. The diets were</p>	<i>OECD recommends that newly hatched larvae are selected that have not yet formed a "C" shape and randomizing the allocation of larvae into the plates for each colony. On Day 1, larva is deposited in cell containing 20 µL diet.</i>

	not heated up to prevent test material breakdown, and were gently mixed to ensure a homogenous diet. On days 3, 4, 5, and 6, a single sample was collected from all test substance concentrations and control for confirmation analysis.	
Bees randomly or impartially assigned to test groups	Yes, larvae were randomly assigned to treatment groups prior to dosing.	<p>Meets standard.</p> <p><i>OECD recommends that each group of a minimum of 12 larvae from each of the three colonies is considered a replicate for a given treatment level and identified as such on the microplate.</i></p>
Control	Untreated diet. 36 negative control larvae.	<p>Meets standard.</p> <p><i>OECD recommends 12 larvae x 3 colonies=36 larvae minimum and that control mortality from Day 4 to Day 7 should be ≤15%.</i></p>
Solvent control	None.	<p>N/A</p> <p><i>OECD recommends maximum of 5%.</i></p>
Reference Toxicant	Dimethoate, tested at a nominal dose and concentration of 7.39 µg ai/larva and 46.3 mg ai/kg, respectively. 36 reference larvae per toxicant.	<p>Meets standard.</p> <p><i>OECD recommends technical grade dimethoate at dose of 8.8 ± 0.5 µg a.i./larva. Mortality should be ≥50% at D7 for toxic reference.</i></p>
Total observation period and frequency of interim observations	Mortality was observed and recorded daily after the first day of exposure. Cells	<p><i>OECD recommends that following chemical exposure on Day 4,</i></p>

	<p>containing dead larvae were removed from plates. Uneaten diet was recorded on Days 7 and 8. Any larvae that failed to consume the diet by Day 8 were considered living for larval survival, but were removed from the study and recorded as dead for pupal survival.</p>	<p><i>mortalities are checked at time of feeding on Days 5, 6, 7, 8 and 15. The presence of uneaten food on Day 8 should be qualitatively recorded. Alive adult bees and dead adults which have left their cell are recorded on Day 22 as well as the number of emerged and non-emerged bees. Other observations (e.g. larval appearance and size, behavior, morphological differences and any other adverse effects after emergence) should be recorded qualitatively.</i></p>
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12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes. The data and report were produced and compiled in accordance with the Good Laboratory Practice Standards as specified in 40 CFR Part 160.
Observed adverse effects on bees at respective dosages	On Day 7 and 8, uneaten diet and reduced body size was recorded. By Day 20, all bees were recorded as either dead or emerged.
Control and Solvent Control Mortality	<u>Day 8 Cumulative Mortality</u> Negative control: 6% <u>Day 15 Cumulative Mortality</u> Negative control: 17% <u>Day 22 Cumulative Mortality</u> Negative control: 17%
Were raw data included?	Yes.

Guideline Criteria	Reported Information
Analytical Analysis?	Yes, conducted in-house at EAG, Inc. with Liquid Chromatography-Mass Spectrometry/Mass Spectrometry (LC-MS/MS)

Mortality and Effects:

By Day 8, cumulative larval mortality was 6% in the negative control, as compared to mortality of 3% to 100% in the treatment groups (**Table 1**). By Day 15, mortality averaged 17% in the negative control, as compared to mortality of 8% to 100% in the groups exposed to the test material (**Table 2**). By Day 22, adult emergence averaged 83% in the negative control, as compared to emergence that ranged from 0% to 92% in the treatment groups.

Unconsumed diet was noted for one bee for the negative control group. There was no unconsumed diet in the treatment groups.

Table 1. Study Author-Reported Cumulative Honey Bee Mortality Data after Repeated Dietary Exposure to Spiromesifen enol (99.0%).

Mean-Measured Daily Dietary Dose (µg a.i./larva/d)	Number Exposed	Day 4 % Mortality	Day 5 % Mortality	Day 6 % Mortality	Day 7 % Mortality	Day 8 % Mortality
Negative Control	36	0	3	3	3	6
0.028	36	0	0	0	3	3
0.058	36	0	0	0	0	3
0.12	36	8	14	31	33	36
0.24	36	39	67	72	81	81
0.50	36	44	100	100	100	100
0.80	36	53	94	100	100	100
Nominal Dose Dimethoate 7.39 µg ai/larva	36	8	31	58	72	81

Table 2. Study Author-Reported Cumulative Honey Bee Pupal Mortality and Adult Emergence Data after Repeated Dietary Exposure to Spiromesifen enol (99.0%).

Mean-Measured Daily Dietary Dose (μg a.i./larva/d)	Number Exposed	Day 15 % Mortality (no. dead)	Day 22 Adult % Emergence (no.)
Negative Control	36	17 (6)	83 (30)
0.028	36	11 (4)	86 (31)
0.058	36	8 (3)	92 (33)
0.12	36	42 (15)	53 (19)
0.24	36	92 (33)	8 (3)
0.50	36	100 (36)	0 (0)
0.80	36	100 (36)	0 (0)
Nominal Dose Dimethoate 7.39 μg ai/larva	36	83 (30)	14 (5)

Study Author's Reported Statistical Analysis:

All statistical analyses were performed using CETIS version 1.9.3.0.

The NOAEC/NOAED values were calculated using Williams' test (adult emergence). The EC/ED₅₀ values with 95% confidence intervals were determined using Probit linear regression. Diet consumption was not an analyzed endpoint, and adult weight at emergence was not reported. The study author reported the following, based on the study author-calculated mean-measured diet concentrations and the measured cumulative doses:

Adult Emergence

EC₅₀: 3.1 mg a.i./kg diet
NOAEC: 1.3 mg a.i./kg diet

95% C.I.: 2.4 - 3.7 mg a.i./kg diet
LOAEC: 2.6 mg a.i./kg diet

ED₅₀: 0.54 μg ai/larva
NOAED: 0.23 μg ai/larva

95% C.I.: 0.42 - 0.63 μg ai/larva
LOAED: 0.46 μg ai/larva

Reviewer's Statistical Analysis:

Mortality and emergence data were analyzed using CETIS statistical software version 1.9.5.3 with database backend settings implemented by EFED on 7/25/17. Toxicological endpoints were determined separately based on spromesifen-enol dose (μg ai/larva) and dietary concentration (mg a.i./kg diet).

Treatment data were tested for normality using Shapiro-Wilk's test ($\alpha = 0.01$) and for homogeneity of variance using Levene's test ($\alpha = 0.01$). Larval mortality, pupal mortality, and adult emergence were all homoscedastic, but had non-normal distributions, and were analyzed using Fisher's Exact/Bonferroni-Holm test due to a lack of monotonicity. Statistical comparisons for all endpoints were made between the negative control and the treatment groups. All analyses were conducted at $\alpha = 0.05$ unless specified otherwise.

The LC/LD₅₀ and EC/ED₅₀ values for larval mortality (Day 8) and adult emergence (Day 22) were calculated using linear regression. The LC/LD₅₀ values for pupal mortality (Day 15) were calculated using Untrimmed Spearman-Kaber regression because the nature of the dose response relationship was so steep around the inflection point of the regression curve that linear regression estimated an LC/LD₅₀ value that was equivalent to the NOAEC/L values (which is indicative of a poorly fitting regression model).

	Mortality (Day 8)	Mortality (Day 15)	Adult Emergence (Day 22)
Diet Concentration mg a.i./kg diet	LC ₅₀ : 3.3 95% CI: 2.2 - 4.8 Slope: 3.8 (2.0 - 5.6) NOAEC: 1.3 LOAEC: 2.6	LC ₅₀ : 3.25 95% CI: 2.82-3.73 Slope: N/A NOAEC: 2.6 LOAEC: 5.8	EC ₅₀ : 2.4 95% CI: 1.8 - 3.2 Slope: 3.0 (2.0 - 4.1) NOAEC: 1.3 LOAEC: 2.6
Dietary Dose μg a.i./larva/day	LD ₅₀ : 0.14 95% CI: 0.094 - 0.21 Slope: 3.9 (1.8-6.0) NOAEL: 0.058 LOAEL: 0.12	LD ₅₀ : 0.14 95% CI: 0.13-0.16 Slope: N/A NOAEL: 0.12 LOAEL: 0.24	ED ₅₀ : 0.11 95% CI: 0.078 - 0.14 Slope: 3.1 (2.0 - 4.1) NOAEL: 0.058 LOAEL: 0.12

13. REVIEWER'S COMMENTS:

The in-life phase of this study was conducted from October 1 to October 20, 2018. The reviewer's and the study author's NOAEC values for adult emergence were in complete agreement. The reviewer obtained slightly lower EC₅₀ values than the study author, despite using a similar test (linear regression by the reviewer and probit analysis by the study author). The NOAEL and ED₅₀ values weren't compared because the reviewer used measured daily doses while the study author used measured cumulative doses. The study author did not analyze larval or pupal mortality, which were both affected endpoints in this study. The reviewer's results are presented in the Conclusions and Reviewer's Conclusions sections of this DER.

All three validity criteria were met for the OECD draft guidance followed:

1. Cumulative larval mortality across all control replicates from Day 3 to Day 8 was $\leq 15\%$.
2. Adult emergence across all control replicates on Day 22 was $\geq 70\%$.

3. Cumulative larval mortality in the positive control of Dimethoate on Day 8 was $\geq 50\%$.

14. REVIEWER'S CONCLUSIONS:

All endpoints were significantly affected by the test material in this experiment, but adult emergence on Day 22 was the most sensitive endpoint. There was a significant reduction (37-100%) in emergence in the four highest test levels, resulting in NOAEC and EC₅₀ values of 1.3 and 2.4 mg a.i./kg diet, respectively (corresponding to a NOAEL and ED₅₀ of 0.058 and 0.11 μ g a.i./larva/d, respectively).

This study is **scientifically sound** and is classified as **supplemental**, but may be used quantitatively for risk assessment purposes.

CETIS Summary Report

Report Date: 21 Oct-19 21:06 (p 1 of 3)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:	
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:	
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:	
Test Length:	17d 0h	Taxon:		Source:	Not Reported
					Age:
Sample ID:	03-6616-7534	Code:	50862201 dd	Project:	Insecticide
Sample Date:	03 Oct-18	Material:	Spiromesifen-enol	Source:	Bayer CropScience
Receipt Date:		CAS (PC):		Station:	
Sample Age:	n/a	Client:	CDM Smith		

024875 50862201 measured dd; Record created by: J. Burns

Multiple Comparison Summary

Analysis ID	Endpoint	Comparison Method	✓ NOEL	LOEL	TOEL	TU	PMSD	S
20-2685-9942	Adult Emergence Rate	Cochran-Armitage (N) Trend Test	✓ 0.058	0.12	0.08343		n/a	1
20-9812-7961	Adult Emergence Rate	Fisher Exact/Bonferroni-Holm Test	✓ 0.058	0.12	0.08343		n/a	1
03-9740-6568	Day 15 Mortality	Cochran-Armitage (N) Trend Test	✓ 0.058	0.12	0.08343		n/a	1
03-8585-5129	Day 15 Mortality	Fisher Exact/Bonferroni-Holm Test	0.12	0.24	0.1697		n/a	1
00-4316-3088	Larval Mortality	Cochran-Armitage (N) Trend Test	✓ 0.058	0.12	0.08343		n/a	1
13-3811-5669	Larval Mortality	Fisher Exact/Bonferroni-Holm Test	✓ 0.058	0.12	0.08343		n/a	1

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓ Level	µg/bee/da	95% LCL	95% UCL	TU	S
13-8923-8717	Adult Emergence Rate	GLM: Log-Normal (Probit)	✓ EC5 ✓ EC10 ✓ EC25 ✓ EC50	0.0304 0.04 0.0633 0.105	0.0142 0.0212 0.0405 0.0777	0.046 0.0573 0.0848 0.14		1
09-5818-4128	Adult Emergence Rate	Spearman-Kärber	EC50	0.137	0.12	0.157		1
02-7732-6039	Day 15 Mortality	GLM: Log-Normal (Probit)	LC5 LC10 LC25 LC50	0.0342 0.0445 0.0688 0.112	0.0156 0.0231 0.0436 0.082	0.0516 0.0637 0.0925 0.151		1
19-9377-9153	Day 15 Mortality	Spearman-Kärber	LC50	0.143	0.125	0.163		1
05-2261-9493	Larval Mortality	GLM: Log-Normal (Probit)	LC5 LC10 LC25 LC50	0.0544 0.0673 0.096 0.143	0.0159 0.0245 0.0488 0.0939	0.0851 0.1 0.136 0.214		1
00-9159-2484	Larval Mortality	Spearman-Kärber	LC50	0.154	0.133	0.179		1

CETIS Summary Report

Report Date: 21 Oct-19 21:06 (p 2 of 3)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study**EAG, Inc.****Adult Emergence Rate Summary**

Conc- μ g/been/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	3	0.833	0.833	0.833	0.833	0.833	0.000	0.000	0.00%	0.00%
0.028		3	0.861	0.742	0.981	0.833	0.917	0.028	0.048	5.59%	-3.33%
0.058		3	0.917	0.710	1.000	0.833	1.000	0.048	0.083	9.09%	-10.00%
0.12		3	0.528	0.000	1.000	0.167	0.750	0.182	0.315	59.78%	36.67%
0.24		3	0.083	0.000	0.442	0.000	0.250	0.083	0.144	173.21%	90.00%
0.5		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		100.00%
0.8		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		100.00%

Day 15 Mortality Summary

Conc- μ g/been/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	3	0.167	0.167	0.167	0.167	0.167	0.000	0.000	0.00%	0.00%
0.028		3	0.111	0.000	0.231	0.083	0.167	0.028	0.048	43.30%	-6.67%
0.058		3	0.083	0.000	0.290	0.000	0.167	0.048	0.083	100.00%	-10.00%
0.12		3	0.417	0.000	1.000	0.167	0.833	0.210	0.363	87.18%	30.00%
0.24		3	0.917	0.558	1.000	0.750	1.000	0.083	0.144	15.75%	90.00%
0.5		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%
0.8		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

Larval Mortality Summary

Conc- μ g/been/day	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	N	3	0.056	0.000	0.175	0.000	0.083	0.028	0.048	86.60%	0.00%
0.028		3	0.028	0.000	0.147	0.000	0.083	0.028	0.048	173.21%	-2.94%
0.058		3	0.028	0.000	0.147	0.000	0.083	0.028	0.048	173.21%	-2.94%
0.12		3	0.361	0.000	1.000	0.000	0.833	0.247	0.428	118.42%	32.35%
0.24		3	0.806	0.000	1.000	0.417	1.000	0.194	0.337	41.81%	79.41%
0.5		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%
0.8		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

CETIS Summary ReportReport Date: 21 Oct-19 21:06 (p 3 of 3)
Test Code/ID: 50862201 dd / 11-5098-4213**Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study****EAG, Inc.****Adult Emergence Rate Detail**

Conc- μ g/been/day	Code	Rep 1	Rep 2	Rep 3
0	N	0.833	0.833	0.833
0.028		0.833	0.917	0.833
0.058		0.917	0.833	1.000
0.12		0.750	0.667	0.167
0.24		0.250	0.000	0.000
0.5		0.000	0.000	0.000
0.8		0.000	0.000	0.000

Day 15 Mortality Detail

Conc- μ g/been/day	Code	Rep 1	Rep 2	Rep 3
0	N	0.167	0.167	0.167
0.028		0.167	0.083	0.083
0.058		0.083	0.167	0.000
0.12		0.250	0.167	0.833
0.24		0.750	1.000	1.000
0.5		1.000	1.000	1.000
0.8		1.000	1.000	1.000

Larval Mortality Detail

Conc- μ g/been/day	Code	Rep 1	Rep 2	Rep 3
0	N	0.083	0.083	0.000
0.028		0.083	0.000	0.000
0.058		0.000	0.083	0.000
0.12		0.250	0.000	0.833
0.24		0.417	1.000	1.000
0.5		1.000	1.000	1.000
0.8		1.000	1.000	1.000

CETIS Summary Report

 Report Date: 21 Oct-19 21:07 (p 1 of 2)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study
EAG, Inc.

Batch ID:	17-1782-3927	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:	
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:	
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:	
Test Length:	17d 0h	Taxon:		Source:	Not Reported
					Age:
Sample ID:	21-2607-3371	Code:	50862201 dc	Project:	Insecticide
Sample Date:	03 Oct-18	Material:	Spiromesifen-enol	Source:	Bayer CropScience
Receipt Date:	16 Jul-19 12:59	CAS (PC):		Station:	
Sample Age:	n/a	Client:	CDM Smith		

024875 50862201 measured dc; record created by: J. Burns

Point Estimate Summary

Analysis ID	Endpoint	Point Estimate Method	✓ Level	mg ai/kg	95% LCL	95% UCL	TU	S
12-2535-9716	Adult Emergence Rate	GLM: Log-Normal (Probit)	✓ EC5	0.691	0.341	1.02	1	1
			✓ EC10	0.91	0.506	1.28		
			✓ EC25	1.44	0.955	1.91		
			✓ EC50	2.4	1.8	3.18		
07-9434-0782	Adult Emergence Rate	Spearman-Kärber	EC50	3.11	2.7	3.59	1	1
12-7947-7525	Day 15 Mortality	GLM: Log-Normal (Probit)	LC5	0.775	0.378	1.15		
			LC10	1.01	0.554	1.42		
			LC25	1.56	1.03	2.08		
			LC50	2.55	1.9	3.41		
08-4845-5116	Day 15 Mortality	Spearman-Kärber	LC50	3.25	2.82	3.73	1	1
03-5293-4723	Larval Mortality	GLM: Log-Normal (Probit)	LC5	1.19	0.428	1.83		
			LC10	1.49	0.64	2.18		
			LC25	2.16	1.21	3.02		
			LC50	3.25	2.23	4.8		
20-6937-5380	Larval Mortality	Spearman-Kärber	LC50	3.52	3.01	4.12	1	1

Adult Emergence Rate Summary

Conc-mg ai/kg	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	N	3	0.833	0.833	0.833	0.833	0.833	0.000	0.000	0.00%	0.00%
0.66		3	0.861	0.742	0.981	0.833	0.917	0.028	0.048	5.59%	-3.33%
1.3		3	0.917	0.710	1.000	0.833	1.000	0.048	0.083	9.09%	-10.00%
2.6		3	0.528	0.000	1.000	0.167	0.750	0.182	0.315	59.78%	36.67%
5.8		3	0.083	0.000	0.442	0.000	0.250	0.083	0.144	173.21%	90.00%
12		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		100.00%
21		3	0.000	0.000	0.000	0.000	0.000	0.000	0.000		100.00%

Day 15 Mortality Summary

Conc-mg ai/kg	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	N	3	0.167	0.167	0.167	0.167	0.167	0.000	0.000	0.00%	0.00%
0.66		3	0.111	0.000	0.231	0.083	0.167	0.028	0.048	43.30%	-6.67%
1.3		3	0.083	0.000	0.290	0.000	0.167	0.048	0.083	100.00%	-10.00%
2.6		3	0.417	0.000	1.000	0.167	0.833	0.210	0.363	87.18%	30.00%
5.8		3	0.917	0.558	1.000	0.750	1.000	0.083	0.144	15.75%	90.00%
12		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%
21		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

Larval Mortality Summary

Conc-mg ai/kg	Code	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	% Effect
0	N	3	0.056	0.000	0.175	0.000	0.083	0.028	0.048	86.60%	0.00%
0.66		3	0.028	0.000	0.147	0.000	0.083	0.028	0.048	173.21%	-2.94%
1.3		3	0.028	0.000	0.147	0.000	0.083	0.028	0.048	173.21%	-2.94%
2.6		3	0.361	0.000	1.000	0.000	0.833	0.247	0.428	118.42%	32.35%
5.8		3	0.806	0.000	1.000	0.417	1.000	0.194	0.337	41.81%	79.41%
12		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%
21		3	1.000	1.000	1.000	1.000	1.000	0.000	0.000	0.00%	100.00%

CETIS Summary ReportReport Date: 21 Oct-19 21:07 (p 2 of 2)
Test Code/ID: 50862201 dc / 16-2181-8188**Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study****EAG, Inc.****Adult Emergence Rate Detail**

Conc-mg ai/kg	Code	Rep 1	Rep 2	Rep 3
0	N	0.833	0.833	0.833
0.66		0.833	0.917	0.833
1.3		0.917	0.833	1.000
2.6		0.750	0.667	0.167
5.8		0.250	0.000	0.000
12		0.000	0.000	0.000
21		0.000	0.000	0.000

Day 15 Mortality Detail

Conc-mg ai/kg	Code	Rep 1	Rep 2	Rep 3
0	N	0.167	0.167	0.167
0.66		0.167	0.083	0.083
1.3		0.083	0.167	0.000
2.6		0.250	0.167	0.833
5.8		0.750	1.000	1.000
12		1.000	1.000	1.000
21		1.000	1.000	1.000

Larval Mortality Detail

Conc-mg ai/kg	Code	Rep 1	Rep 2	Rep 3
0	N	0.083	0.083	0.000
0.66		0.083	0.000	0.000
1.3		0.000	0.083	0.000
2.6		0.250	0.000	0.833
5.8		0.417	1.000	1.000
12		1.000	1.000	1.000
21		1.000	1.000	1.000

CETIS Analytical Report

Report Date: 21 Oct-19 21:06 (p 1 of 6)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	20-2685-9942	Endpoint:	Adult Emergence Rate	CETIS Version:	CETISv1.9.5
Analyzed:	21 Oct-19 21:02	Analysis:	STP 2xK Contingency Tables-Numerical Sc	Status Level:	1

Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Data Transform	Alt Hyp	NOEL	LOEL	TOEL	TU
Untransformed	C > T	0.058	0.12	0.08343	

Cochran-Armitage (N) Trend Test

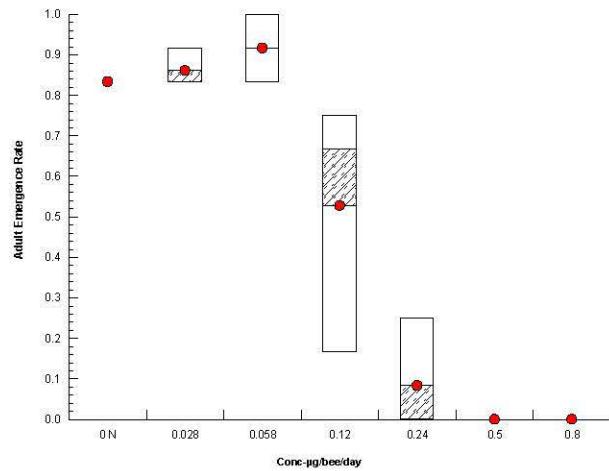
Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α :5%)
Negative Control		0.028	-0.325	Asymp	0.8433	Non-Significant Effect
		0.058	-1.008	Asymp	0.8433	Non-Significant Effect
		0.12*	3.445	Asymp	2.9E-04	Significant Effect
		0.24*	8.348	Asymp	<1.0E-37	Significant Effect
		0.5*	9.939	Asymp	<1.0E-37	Significant Effect
		0.8*	10.629	Asymp	<1.0E-37	Significant Effect

Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α :5%)
Overall Effect	Pearson Chi-Square Test	156	12.6	1.5E-07	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	43.3	11.1	<1.0E-37	Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	2.81	1.64	0.0025	Significant Overdispersion

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	30	6	36	0.833	0.167	0.0%
0.028		31	5	36	0.861	0.139	-3.33%
0.058		33	3	36	0.917	0.0833	-10.0%
0.12		19	17	36	0.528	0.472	36.7%
0.24		3	33	36	0.0833	0.917	90.0%
0.5		0	36	36	0	1	100.0%
0.8		0	36	36	0	1	100.0%

Graphics

CETIS Analytical Report

Report Date: 21 Oct-19 21:06 (p 2 of 6)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

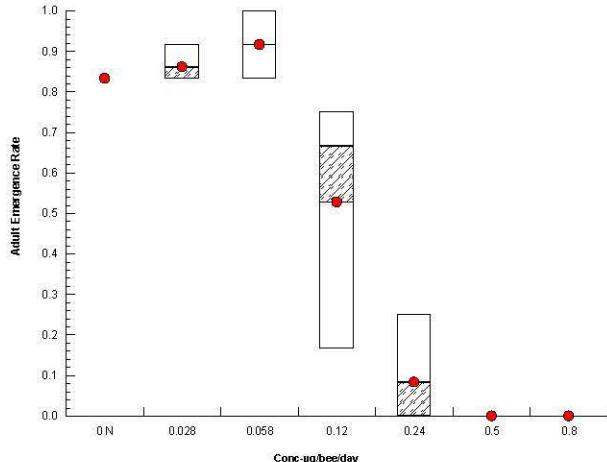
Analysis ID:	20-9812-7961	Endpoint:	Adult Emergence Rate	CETIS Version:	CETISv1.9.5		
Analyzed:	21 Oct-19 21:03	Analysis:	STP 2xK Contingency Tables	Status Level:	1		
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:			
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:			
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:			
Test Length:	17d 0h	Taxon:		Source:	Not Reported		
					Age:		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C > T			0.058	0.12	0.08343	

Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α :5%)
Negative Control		0.028	0.743	Exact	1.0000	Non-Significant Effect
		0.058	0.924	Exact	0.9243	Non-Significant Effect
		0.12*	0.005	Exact	0.0160	Significant Effect
		0.24*	0.000	Exact	1.6E-10	Significant Effect
		0.5*	0.000	Exact	7.1E-14	Significant Effect
		0.8*	0.000	Exact	7.1E-14	Significant Effect

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	30	6	36	0.833	0.167	0.0%
0.028		31	5	36	0.861	0.139	-3.33%
0.058		33	3	36	0.917	0.0833	-10.0%
0.12		19	17	36	0.528	0.472	36.7%
0.24		3	33	36	0.0833	0.917	90.0%
0.5		0	36	36	0	1	100.0%
0.8		0	36	36	0	1	100.0%

Graphics

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	03-8585-5129	Endpoint:	Day 15 Mortality	CETIS Version:	CETISv1.9.5		
Analyzed:	21 Oct-19 21:01	Analysis:	STP 2xK Contingency Tables	Status Level:	1		
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:			
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:			
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:			
Test Length:	17d 0h	Taxon:		Source:	Not Reported		
					Age:		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C < T			0.12	0.24	0.1697	

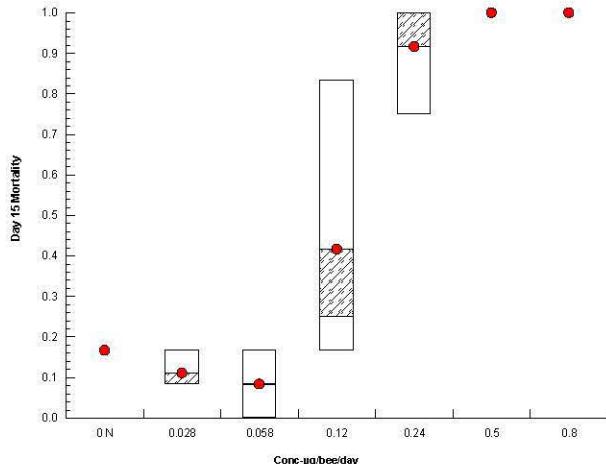
Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α :5%)
Negative Control		0.028	0.846	Exact	1.0000	Non-Significant Effect
		0.058	0.924	Exact	0.9243	Non-Significant Effect
		0.12	0.018	Exact	0.0550	Non-Significant Effect
		0.24*	0.000	Exact	1.6E-10	Significant Effect
		0.5*	0.000	Exact	7.1E-14	Significant Effect
		0.8*	0.000	Exact	7.1E-14	Significant Effect

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	30	6	36	0.833	0.167	0.0%
0.028		32	4	36	0.889	0.111	33.3%
0.058		33	3	36	0.917	0.0833	50.0%
0.12		21	15	36	0.583	0.417	-150.0%
0.24		3	33	36	0.0833	0.917	-450.0%
0.5		0	36	36	0	1	-500.0%
0.8		0	36	36	0	1	-500.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	03-9740-6568	Endpoint:	Day 15 Mortality	CETIS Version:	CETISv1.9.5		
Analyzed:	21 Oct-19 21:01	Analysis:	STP 2xK Contingency Tables-Numerical Sc	Status Level:	1		
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:			
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:			
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:			
Test Length:	17d 0h	Taxon:		Source:	Not Reported		
					Age:		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C < T			0.058	0.12	0.08343	

Cochran-Armitage (N) Trend Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control		0.028	-0.676	Asymp	0.8510	Non-Significant Effect
		0.058	-1.041	Asymp	0.8510	Non-Significant Effect
		0.12*	3.052	Asymp	0.0011	Significant Effect
		0.24*	8.432	Asymp	<1.0E-37	Significant Effect
		0.5*	10.125	Asymp	<1.0E-37	Significant Effect
		0.8*	10.830	Asymp	<1.0E-37	Significant Effect

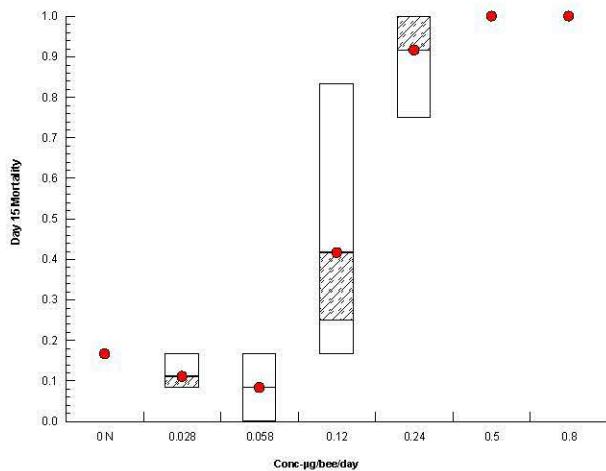
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Overall Effect	Pearson Chi-Square Test	160	12.6	1.3E-07	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	43.2	11.1	<1.0E-37	Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	4.28	1.64	9.5E-06	Significant Overdispersion

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	30	6	36	0.833	0.167	0.0%
0.028		32	4	36	0.889	0.111	33.3%
0.058		33	3	36	0.917	0.0833	50.0%
0.12		21	15	36	0.583	0.417	-150.0%
0.24		3	33	36	0.0833	0.917	-450.0%
0.5		0	36	36	0	1	-500.0%
0.8		0	36	36	0	1	-500.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	13-3811-5669	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5		
Analyzed:	21 Oct-19 21:01	Analysis:	STP 2xK Contingency Tables	Status Level:	1		
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:			
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:			
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:			
Test Length:	17d 0h	Taxon:		Source:	Not Reported		
					Age:		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C < T			0.058	0.12	0.08343	

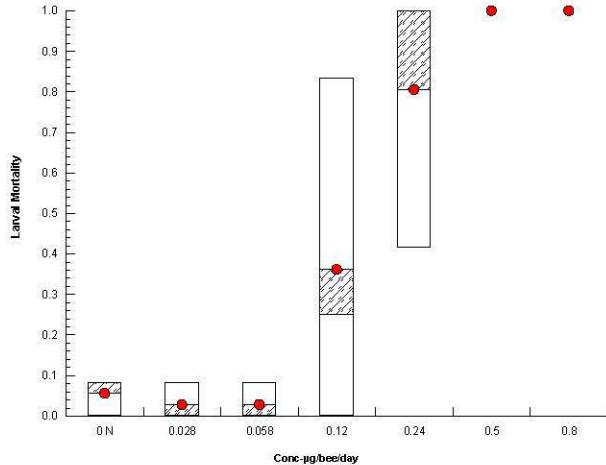
Fisher Exact/Bonferroni-Holm Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision(α :5%)
Negative Control		0.028	0.880	Exact	1.0000	Non-Significant Effect
		0.058	0.880	Exact	1.0000	Non-Significant Effect
		0.12*	0.001	Exact	0.0041	Significant Effect
		0.24*	0.000	Exact	9.6E-11	Significant Effect
		0.5*	0.000	Exact	9.5E-18	Significant Effect
		0.8*	0.000	Exact	9.5E-18	Significant Effect

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	34	2	36	0.944	0.0556	0.0%
0.028		35	1	36	0.972	0.0278	50.0%
0.058		35	1	36	0.972	0.0278	50.0%
0.12		23	13	36	0.639	0.361	-550.0%
0.24		7	29	36	0.194	0.806	-1350.0%
0.5		0	36	36	0	1	-1700.0%
0.8		0	36	36	0	1	-1700.0%

Graphics



Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	00-4316-3088	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5		
Analyzed:	21 Oct-19 21:01	Analysis:	STP 2xK Contingency Tables-Numerical Sc	Status Level:	1		
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:			
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:			
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:			
Test Length:	17d 0h	Taxon:		Source:	Not Reported		
					Age:		
Data Transform	Alt Hyp			NOEL	LOEL	TOEL	TU
Untransformed	C < T			0.058	0.12	0.08343	

Cochran-Armitage (N) Trend Test

Control	vs	Group	Test Stat	P-Type	P-Value	Decision($\alpha:5\%$)
Negative Control		0.028	-0.585	Asymp	0.7250	Non-Significant Effect
		0.058	-0.598	Asymp	0.7250	Non-Significant Effect
		0.12*	4.469	Asymp	3.9E-06	Significant Effect
		0.24*	9.017	Asymp	<1.0E-37	Significant Effect
		0.5*	11.164	Asymp	<1.0E-37	Significant Effect
		0.8*	11.907	Asymp	<1.0E-37	Significant Effect

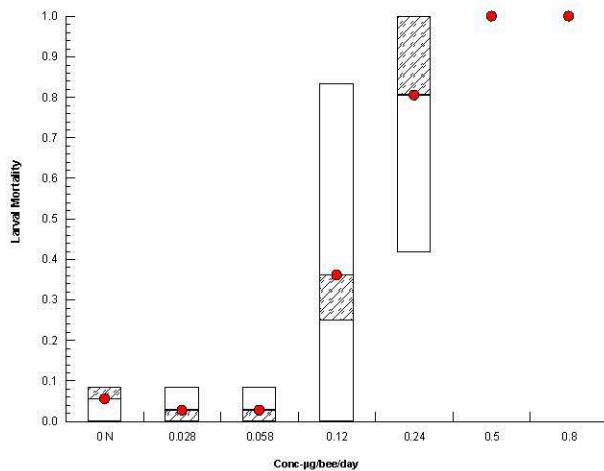
Auxiliary Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Overall Effect	Pearson Chi-Square Test	181	12.6	<1.0E-37	Significant Overall Effect
Nonlinearity	Chi-Square Lack of Fit Test	38.8	11.1	3.1E-07	Significant Lack of Linearity
Overdispersion	Tarone C(α) Binomial Overdispersion Test	6.83	1.64	<1.0E-37	Significant Overdispersion

Data Summary

Conc- μ g/bee/day	Code	NR	R	NR + R	Prop NR	Prop R	% Effect
0	N	34	2	36	0.944	0.0556	0.0%
0.028		35	1	36	0.972	0.0278	50.0%
0.058		35	1	36	0.972	0.0278	50.0%
0.12		23	13	36	0.639	0.361	-550.0%
0.24		7	29	36	0.194	0.806	-1350.0%
0.5		0	36	36	0	1	-1700.0%
0.8		0	36	36	0	1	-1700.0%

Graphics



CETIS Analytical Report

Report Date: 21 Oct-19 21:05 (p 1 of 6)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	13-8923-8717	Endpoint:	Adult Emergence Rate	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 12:54	Analysis:	Linear Regression (GLM)	Status Level:	1

Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision($\alpha:5\%$)
8	-28.5	61.8	62.8	-0.978	0.328	0.938		2.95	0.0656	Non-Significant Lack of Fit

Point Estimates

Level	$\mu\text{g}/\text{bee}/\text{da}$	95% LCL	95% UCL
EC5	0.0304	0.0142	0.046
EC10	0.04	0.0212	0.0573
EC25	0.0633	0.0405	0.0848
EC50	0.105	0.0777	0.14

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	2.98	0.503	1.92	4.05	5.93	2.1E-05	Significant Parameter
Slope	3.05	0.496	2	4.1	6.15	1.4E-05	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	528	528	1	260	<1.0E-37	Significant
Lack of Fit	16.1	4.03	4	2.95	0.0656	Non-Significant
Pure Error	16.4	1.37	12			
Residual	32.5	2.03	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	35.2	26.3	0.0038	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	32.5	26.3	0.0086	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.858	4.39	0.5573	Equal Variances
	Anderson-Darling A2 Normality Test	0.383	2.49	0.4024	Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.951	0.897	0.4335	Normal Distribution
	Tarone C(α) Binomial Overdispersion	2.81	1.64	0.0025	Significant Overdispersion

Adult Emergence Rate Summary

Calculated Variate(A/B)

Conc- $\mu\text{g}/\text{bee}/\text{day}$	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.028		3	0.861	0.833	0.917	0.028	0.048	5.59%	0.0%	31	36
0.058		3	0.917	0.833	1.000	0.048	0.083	9.09%	-6.45%	33	36
0.12		3	0.528	0.167	0.750	0.182	0.315	59.80%	38.7%	19	36
0.24		3	0.083	0.000	0.250	0.083	0.144	173.00%	90.3%	3	36
0.5		3	0.000	0.000	0.000	0.000	0.000		100.0%	0	36
0.8		3	0.000	0.000	0.000	0.000	0.000		100.0%	0	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

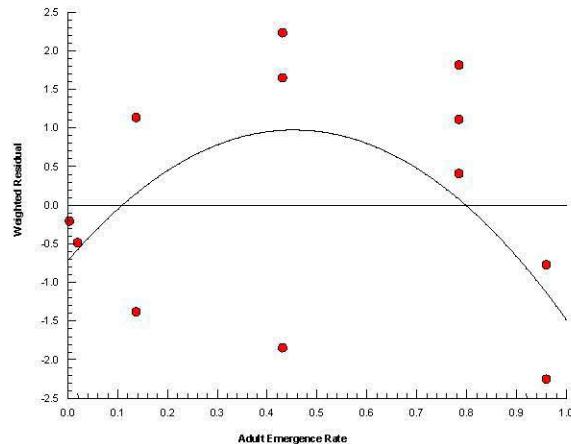
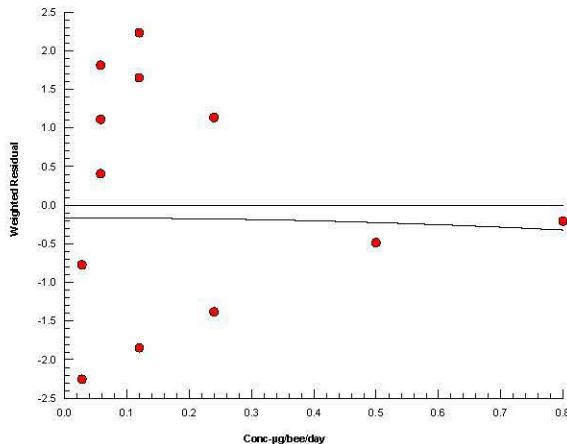
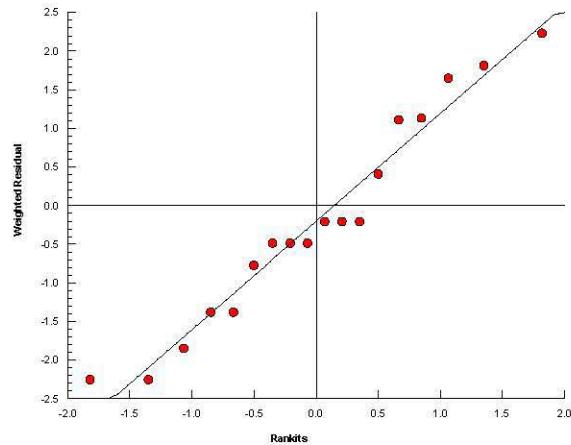
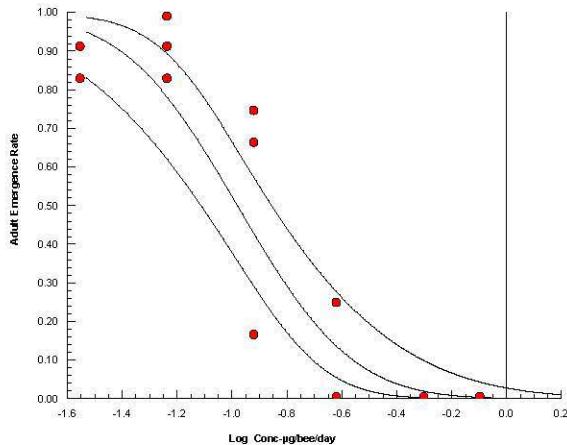
EAG, Inc.

 Analysis ID: 13-8923-8717
 Analyzed: 16 Jul-19 12:54

 Endpoint: Adult Emergence Rate
 Analysis: Linear Regression (GLM)

 CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:05 (p 3 of 6)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	02-7732-6039	Endpoint:	Day 15 Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 12:56	Analysis:	Linear Regression (GLM)	Status Level:	1

Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSE	F Stat	P-Value	Decision($\alpha:5\%$)
8	-29.3	63.4	64.4	-0.951	0.313	0.954		2.39	0.1090	Non-Significant Lack of Fit

Point Estimates

Level	$\mu\text{g}/\text{bee}/\text{da}$	95% LCL	95% UCL
LC5	0.0342	0.0156	0.0516
LC10	0.0445	0.0231	0.0637
LC25	0.0688	0.0436	0.0925
LC50	0.112	0.082	0.151

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	3.04	0.544	1.89	4.19	5.59	4.0E-05	Significant Parameter
Slope	3.2	0.548	2.03	4.36	5.83	2.6E-05	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	800	800	1	356	<1.0E-37	Significant
Lack of Fit	15.9	3.98	4	2.39	0.1089	Non-Significant
Pure Error	20	1.67	12			
Residual	35.9	2.25	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	37.7	26.3	0.0017	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	35.9	26.3	0.0030	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.846	4.39	0.5634	Equal Variances
	Anderson-Darling A2 Normality Test	0.329	2.49	0.5300	Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.973	0.897	0.8542	Normal Distribution
	Tarone C(α) Binomial Overdispersion	4.28	1.64	9.5E-06	Significant Overdispersion

Day 15 Mortality Summary

Calculated Variate(A/B)

Conc- $\mu\text{g}/\text{bee}/\text{day}$	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.028		3	0.111	0.083	0.167	0.028	0.048	43.30%	0.0%	4	36
0.058		3	0.083	0.000	0.167	0.048	0.083	100.00%	-3.12%	3	36
0.12		3	0.417	0.167	0.833	0.210	0.363	87.20%	34.4%	15	36
0.24		3	0.917	0.750	1.000	0.083	0.144	15.70%	90.6%	33	36
0.5		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
0.8		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

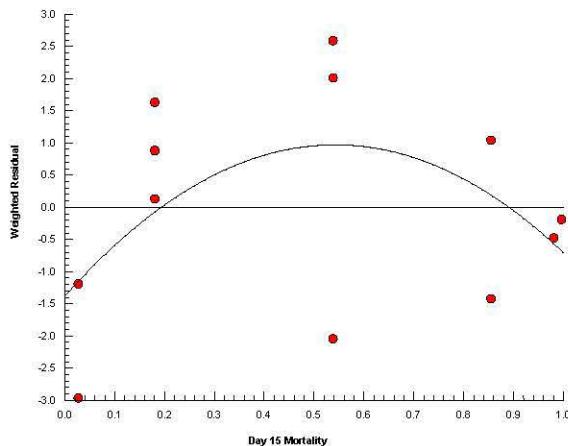
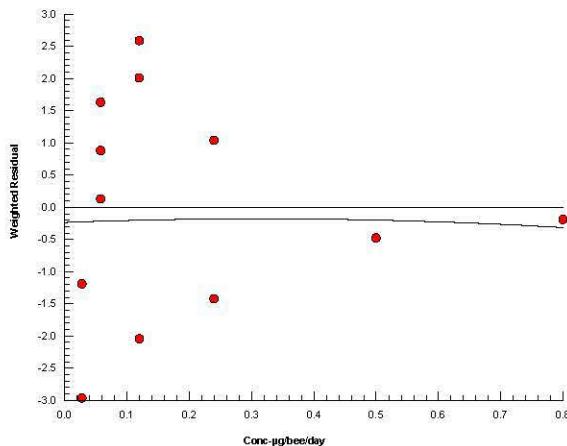
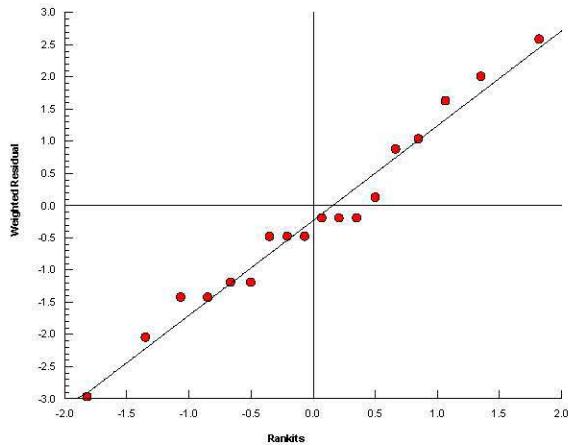
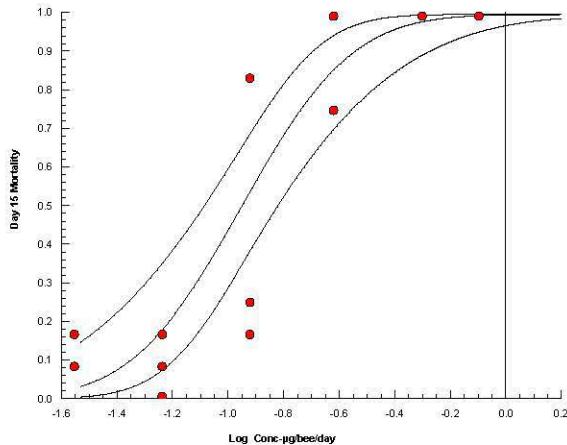
EAG, Inc.

 Analysis ID: 02-7732-6039
 Analyzed: 16 Jul-19 12:56

 Endpoint: Day 15 Mortality
 Analysis: Linear Regression (GLM)

 CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:05 (p 5 of 6)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	05-2261-9493	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 12:58	Analysis:	Linear Regression (GLM)	Status Level:	1

Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision($\alpha:5\%$)
7	-31.8	68.3	69.3	-0.846	0.255	0.993		0.506	0.7330	Non-Significant Lack of Fit

Point Estimates

Level	$\mu\text{g}/\text{bee}/\text{da}$	95% LCL	95% UCL
LC5	0.0544	0.0159	0.0851
LC10	0.0673	0.0245	0.1
LC25	0.096	0.0488	0.136
LC50	0.143	0.0939	0.214

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	3.32	0.874	1.47	5.18	3.8	0.0016	Significant Parameter
Slope	3.93	0.988	1.84	6.02	3.98	0.0011	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	9500	9500	1	2250	<1.0E-37	Significant
Lack of Fit	9.73	2.43	4	0.506	0.7325	Non-Significant
Pure Error	57.7	4.81	12			
Residual	67.4	4.21	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	51.6	26.3	1.3E-05	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	67.4	26.3	<1.0E-37	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.764	4.39	0.6073	Equal Variances
	Anderson-Darling A2 Normality Test	0.873	2.49	0.0251	Non-Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.916	0.897	0.1104	Normal Distribution
	Tarone C(α) Binomial Overdispersion	6.83	1.64	<1.0E-37	Significant Overdispersion

Larval Mortality Summary Calculated Variate(A/B)

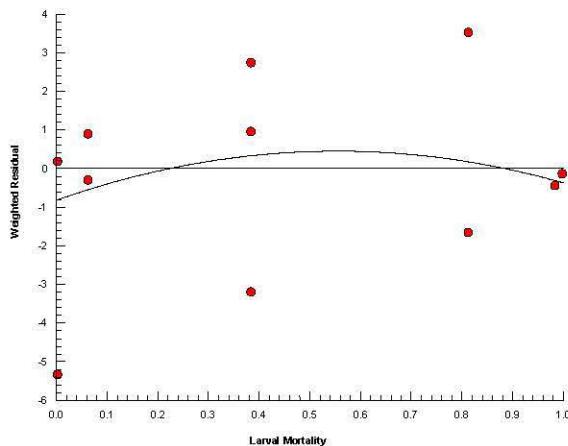
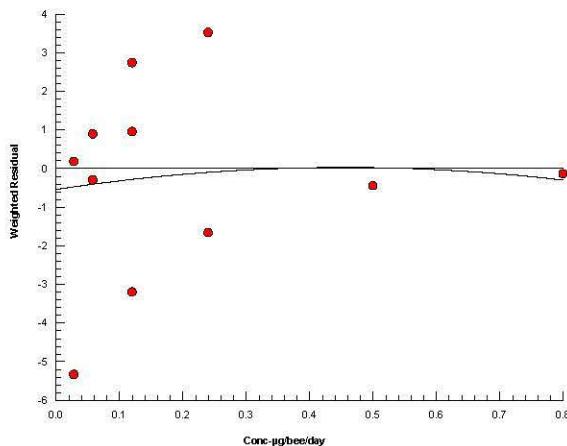
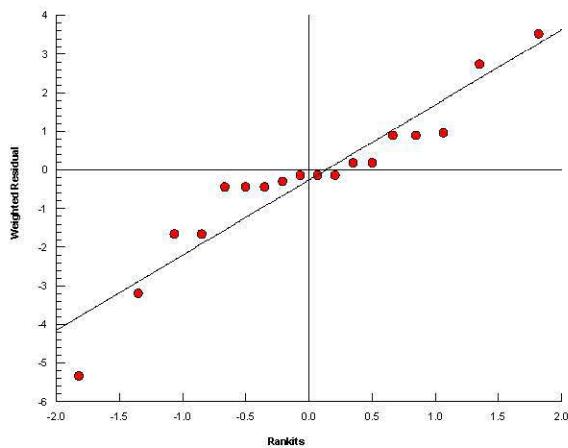
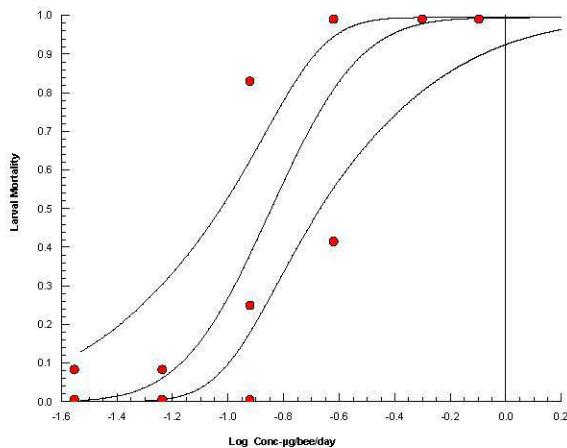
Conc- $\mu\text{g}/\text{bee}/\text{day}$	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.028		3	0.028	0.000	0.083	0.028	0.048	173.00%	0.0%	1	36
0.058		3	0.028	0.000	0.083	0.028	0.048	173.00%	0.0%	1	36
0.12		3	0.361	0.000	0.833	0.247	0.428	118.00%	34.3%	13	36
0.24		3	0.806	0.417	1.000	0.194	0.337	41.80%	80.0%	29	36
0.5		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
0.8		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 05-2261-9493
Analyzed: 16 Jul-19 12:58Endpoint: Larval Mortality
Analysis: Linear Regression (GLM)CETIS Version: CETISv1.9.5
Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:05 (p 1 of 3)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 09-5818-4128 **Endpoint:** Adult Emergence Rate
Analyzed: 16 Jul-19 12:54 **Analysis:** Untrimmed Spearman-Kärber

CETIS Version: CETISv1.9.5
Status Level: 1

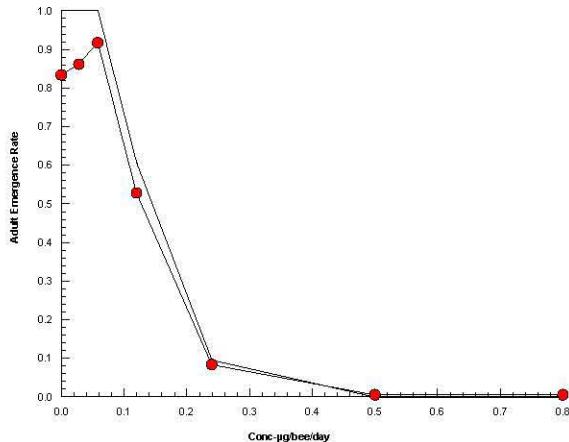
Batch ID: 09-0428-0410 **Test Type:** OECD 2014 HB Larval Repeat Exp
Start Date: 03 Oct-18 **Protocol:** Larval Chronic Oral Toxicity, 21-day Study
Ending Date: 20 Oct-18 **Species:** Apis mellifera
Test Length: 17d 0h **Taxon:**

Analyst:
Diluent:
Brine:
Source: Not Reported **Age:**

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.167	0.00%	-0.862	0.0294	0.137	0.12	0.157

Adult Emergence Rate Summary			Calculated Variate(A/B)					Isotonic Variate			
Conc- μ g/bee/day	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.833	0.833	0.833	0.000	0.00%	0.0%	30/36	0.87	0.0%
0.028		3	0.861	0.833	0.917	0.048	5.59%	-3.33%	31/36	0.87	0.0%
0.058		3	0.917	0.833	1.000	0.083	9.09%	-10.0%	33/36	0.87	0.0%
0.12		3	0.528	0.167	0.750	0.315	59.80%	36.7%	19/36	0.528	39.4%
0.24		3	0.083	0.000	0.250	0.144	173.00%	90.0%	3/36	0.0833	90.4%
0.5		3	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%
0.8		3	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%

Graphics

CETIS Analytical Report

Report Date: 21 Oct-19 21:05 (p 2 of 3)
 Test Code/ID: 50862201 dd / 11-5098-4213

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 19-9377-9153 **Endpoint:** Day 15 Mortality
Analyzed: 16 Jul-19 12:56 **Analysis:** Untrimmed Spearman-Kärber

CETIS Version: CETISv1.9.5
Status Level: 1

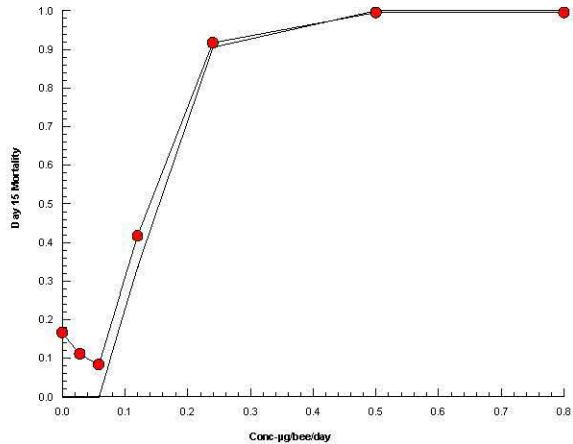
Batch ID: 09-0428-0410 **Test Type:** OECD 2014 HB Larval Repeat Exp
Start Date: 03 Oct-18 **Protocol:** Larval Chronic Oral Toxicity, 21-day Study
Ending Date: 20 Oct-18 **Species:** Apis mellifera
Test Length: 17d 0h **Taxon:**

Analyst:
Diluent:
Brine:
Source: Not Reported **Age:**

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.167	0.00%	-0.845	0.0286	0.143	0.125	0.163

Day 15 Mortality Summary			Calculated Variate(A/B)					Isotonic Variate			
Conc- μ g/bee/day	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.167	0.167	0.167	0.000	0.00%	0.0%	6/36	0.12	0.0%
0.028		3	0.111	0.083	0.167	0.048	43.30%	-6.67%	4/36	0.12	0.0%
0.058		3	0.083	0.000	0.167	0.083	100.00%	-10.0%	3/36	0.12	0.0%
0.12		3	0.417	0.167	0.833	0.363	87.20%	30.0%	15/36	0.417	33.7%
0.24		3	0.917	0.750	1.000	0.144	15.70%	90.0%	33/36	0.917	90.5%
0.5		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
0.8		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

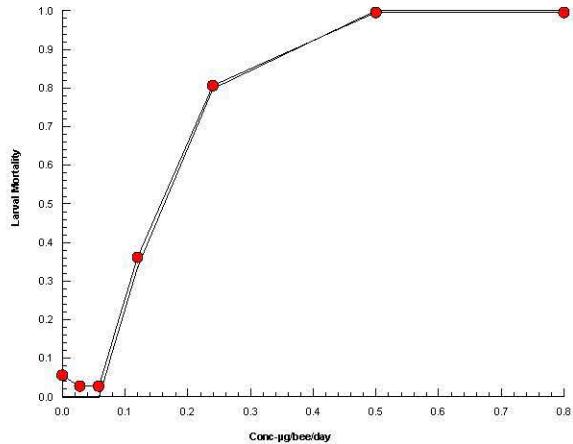
Analysis ID:	00-9159-2484	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 12:58	Analysis:	Untrimmed Spearman-Kärber	Status Level:	1
Batch ID:	09-0428-0410	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:	
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:	
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:	
Test Length:	17d 0h	Taxon:		Source:	Not Reported
					Age:

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.0556	0.00%	-0.812	0.0319	0.154	0.133	0.179

Larval Mortality Summary			Calculated Variate(A/B)						Isotonic Variate		
Conc- $\mu\text{g}/\text{bee/day}$	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.056	0.000	0.083	0.048	86.60%	0.0%	2/36	0.037	0.0%
0.028		3	0.028	0.000	0.083	0.048	173.00%	-2.94%	1/36	0.037	0.0%
0.058		3	0.028	0.000	0.083	0.048	173.00%	-2.94%	1/36	0.037	0.0%
0.12		3	0.361	0.000	0.833	0.428	118.00%	32.4%	13/36	0.361	33.7%
0.24		3	0.806	0.417	1.000	0.337	41.80%	79.4%	29/36	0.806	79.8%
0.5		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
0.8		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics



CETIS Analytical Report

Report Date: 21 Oct-19 21:07 (p 1 of 6)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	12-2535-9716	Endpoint:	Adult Emergence Rate	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 13:04	Analysis:	Linear Regression (GLM)	Status Level:	1

Batch ID:	17-1782-3927	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision($\alpha:5\%$)
7	-27.3	59.3	60.3	0.38	0.329	0.939		2.35	0.1130	Non-Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
EC5	0.691	0.341	1.02
EC10	0.91	0.506	1.28
EC25	1.44	0.955	1.91
EC50	2.4	1.8	3.18

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	-1.16	0.249	-1.68	-0.629	-4.65	2.7E-04	Significant Parameter
Slope	3.04	0.477	2.03	4.05	6.38	9.1E-06	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	485	485	1	262	<1.0E-37	Significant
Lack of Fit	13	3.26	4	2.35	0.1131	Non-Significant
Pure Error	16.6	1.39	12			
Residual	29.7	1.85	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	32.7	26.3	0.0082	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	29.7	26.3	0.0198	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.85	4.39	0.5613	Equal Variances
	Anderson-Darling A2 Normality Test	0.452	2.49	0.2766	Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.937	0.897	0.2601	Normal Distribution
	Tarone C(α) Binomial Overdispersion	2.81	1.64	0.0025	Significant Overdispersion

Adult Emergence Rate Summary

Calculated Variate(A/B)

Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.66		3	0.861	0.833	0.917	0.028	0.048	5.59%	0.0%	31	36
1.3		3	0.917	0.833	1.000	0.048	0.083	9.09%	-6.45%	33	36
2.6		3	0.528	0.167	0.750	0.182	0.315	59.80%	38.7%	19	36
5.8		3	0.083	0.000	0.250	0.083	0.144	173.00%	90.3%	3	36
12		3	0.000	0.000	0.000	0.000	0.000		100.0%	0	36
21		3	0.000	0.000	0.000	0.000	0.000		100.0%	0	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

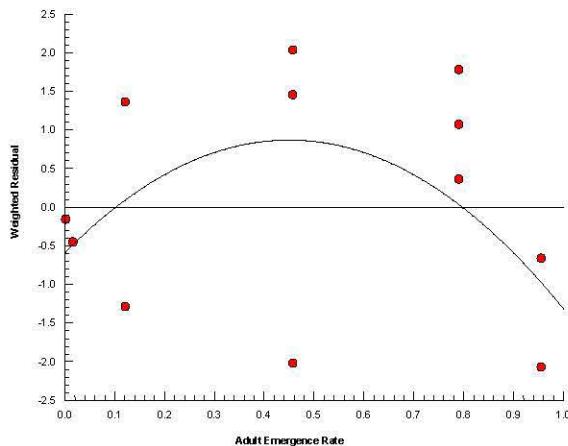
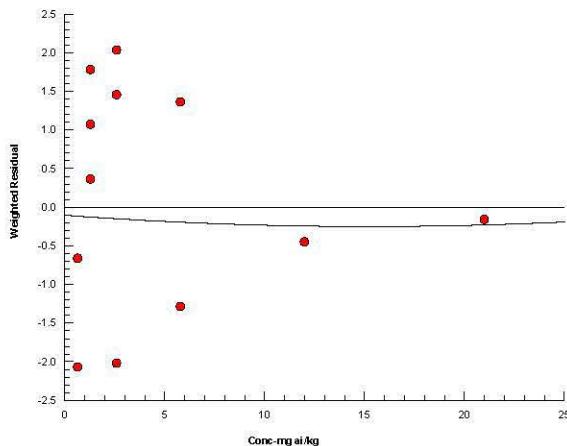
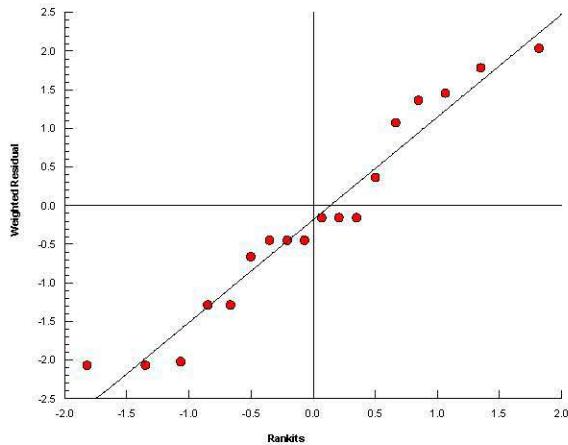
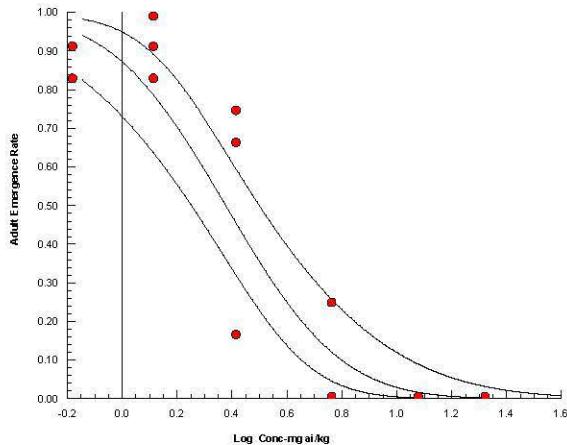
EAG, Inc.

 Analysis ID: 12-2535-9716
 Analyzed: 16 Jul-19 13:04

 Endpoint: Adult Emergence Rate
 Analysis: Linear Regression (GLM)

 CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:07 (p 3 of 6)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	12-7947-7525	Endpoint:	Day 15 Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 13:05	Analysis:	Linear Regression (GLM)	Status Level:	1

Batch ID:	17-1782-3927	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:
Test Length:	17d 0h	Taxon:		Source: Not Reported Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision($\alpha:5\%$)
7	-27.9	60.7	61.7	0.406	0.314	0.954		1.85	0.1840	Non-Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
LC5	0.775	0.378	1.15
LC10	1.01	0.554	1.42
LC25	1.56	1.03	2.08
LC50	2.55	1.9	3.41

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	-1.29	0.278	-1.88	-0.704	-4.66	2.6E-04	Significant Parameter
Slope	3.18	0.523	2.07	4.29	6.09	1.6E-05	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	715	715	1	351	<1.0E-37	Significant
Lack of Fit	12.4	3.11	4	1.85	0.1842	Non-Significant
Pure Error	20.2	1.68	12			
Residual	32.6	2.04	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	35	26.3	0.0040	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	32.6	26.3	0.0084	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.844	4.39	0.5644	Equal Variances
	Anderson-Darling A2 Normality Test	0.346	2.49	0.4873	Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.969	0.897	0.7761	Normal Distribution
	Tarone C(α) Binomial Overdispersion	4.28	1.64	9.5E-06	Significant Overdispersion

Day 15 Mortality Summary

Calculated Variate(A/B)

Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.66		3	0.111	0.083	0.167	0.028	0.048	43.30%	0.0%	4	36
1.3		3	0.083	0.000	0.167	0.048	0.083	100.00%	-3.12%	3	36
2.6		3	0.417	0.167	0.833	0.210	0.363	87.20%	34.4%	15	36
5.8		3	0.917	0.750	1.000	0.083	0.144	15.70%	90.6%	33	36
12		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
21		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

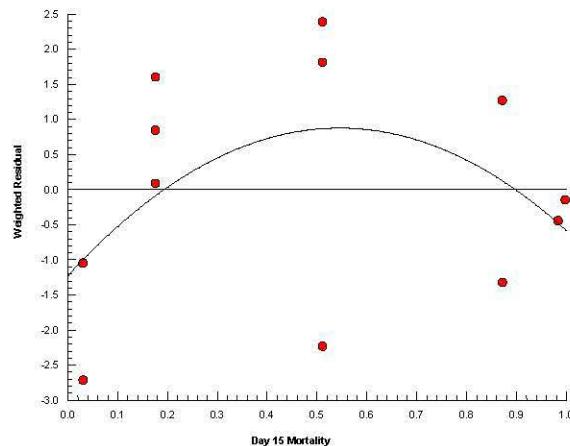
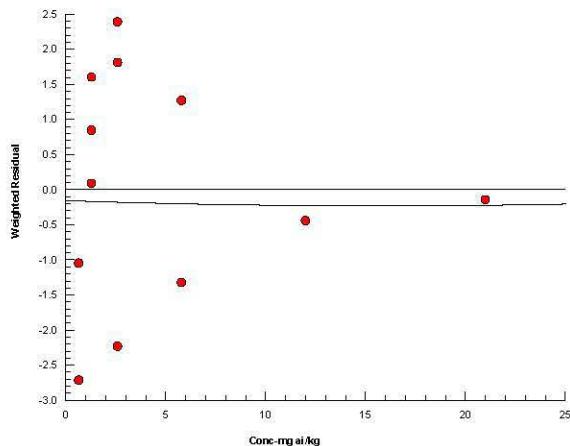
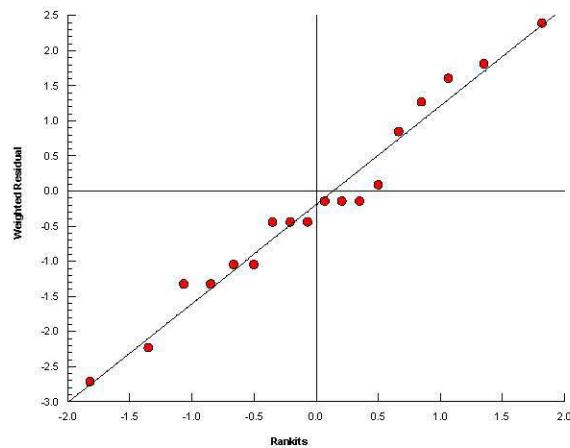
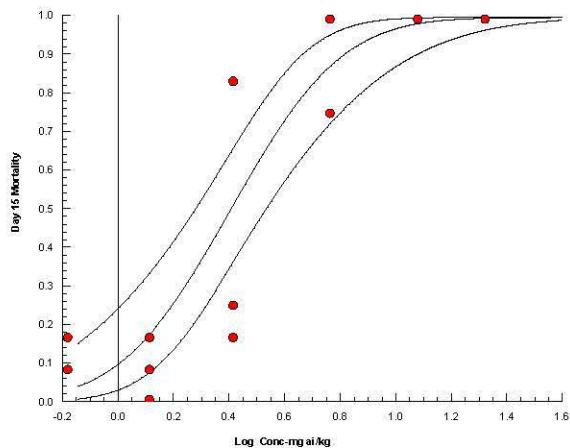
EAG, Inc.

 Analysis ID: 12-7947-7525
 Analyzed: 16 Jul-19 13:05

 Endpoint: Day 15 Mortality
 Analysis: Linear Regression (GLM)

 CETIS Version: CETISv1.9.5
 Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:07 (p 5 of 6)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	03-5293-4723	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 13:06	Analysis:	Linear Regression (GLM)	Status Level:	1
Batch ID:	17-1782-3927	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:	
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:	
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:	
Test Length:	17d 0h	Taxon:		Source:	Not Reported
					Age:

Linear Regression Options

Model Name	Link Function	Threshold Option	Thresh	Optimize	Pooled	Het Corr	Weighted
Log-Normal (Probit) $\eta = \text{inv } \Phi[\pi]$		Zero Threshold	0	No	No	Yes	Yes

Regression Summary

Iters	LL	AICc	BIC	Mu	Sigma	Adj R2	PMSD	F Stat	P-Value	Decision($\alpha:5\%$)
7	-31.4	67.7	68.6	0.512	0.265	0.99		0.35	0.8390	Non-Significant Lack of Fit

Point Estimates

Level	mg ai/kg	95% LCL	95% UCL
LC5	1.19	0.428	1.83
LC10	1.49	0.64	2.18
LC25	2.16	1.21	3.02
LC50	3.25	2.23	4.8

Regression Parameters

Parameter	Estimate	Std Error	95% LCL	95% UCL	t Stat	P-Value	Decision($\alpha:5\%$)
Intercept	-1.93	0.505	-3	-0.863	-3.83	0.0015	Significant Parameter
Slope	3.77	0.856	1.96	5.59	4.41	4.4E-04	Significant Parameter

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision($\alpha:5\%$)
Model	5780	5780	1	1600	<1.0E-37	Significant
Lack of Fit	6.02	1.51	4	0.35	0.8391	Non-Significant
Pure Error	51.6	4.3	12			
Residual	57.7	3.6	16			

Residual Analysis

Attribute	Method	Test Stat	Critical	P-Value	Decision($\alpha:5\%$)
Model Fit	Likelihood Ratio GOF Test	50.9	26.3	1.6E-05	Significant Heterogeneity
	Pearson Chi-Sq GOF Test	57.7	26.3	1.3E-06	Significant Heterogeneity
Variance Distribution	Mod Levene Equality of Variance	0.828	4.39	0.5728	Equal Variances
	Anderson-Darling A2 Normality Test	0.783	2.49	0.0419	Non-Normal Distribution
Overdispersion	Shapiro-Wilk W Normality Test	0.931	0.897	0.2010	Normal Distribution
	Tarone C(α) Binomial Overdispersion	6.83	1.64	<1.0E-37	Significant Overdispersion

Larval Mortality Summary

Calculated Variate(A/B)

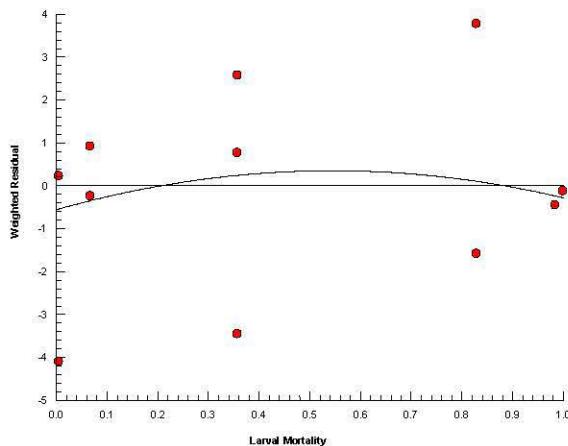
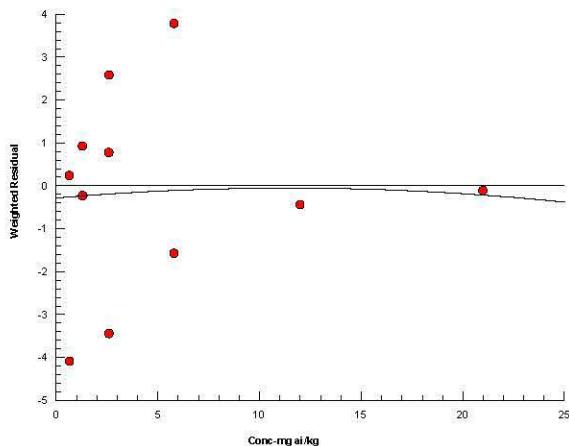
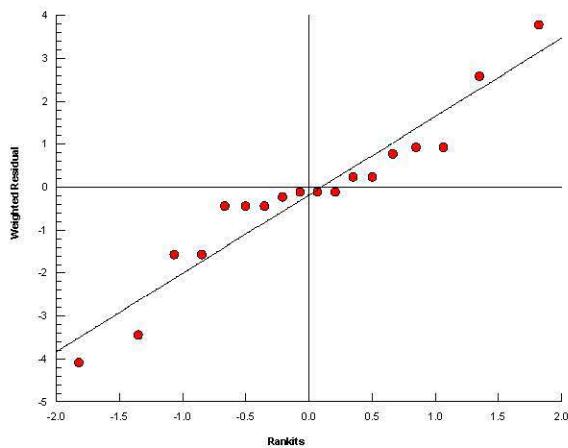
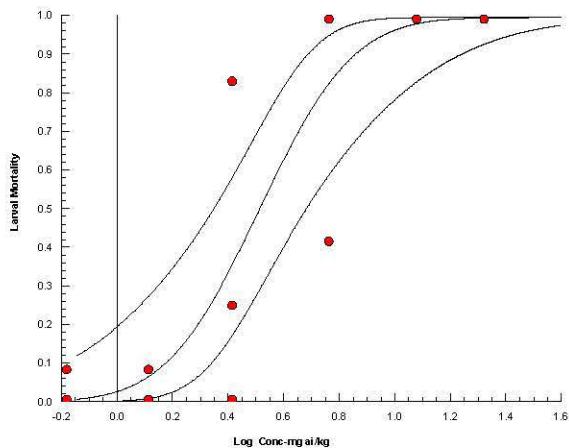
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Err	Std Dev	CV%	%Effect	A	B
0.66		3	0.028	0.000	0.083	0.028	0.048	173.00%	0.0%	1	36
1.3		3	0.028	0.000	0.083	0.028	0.048	173.00%	0.0%	1	36
2.6		3	0.361	0.000	0.833	0.247	0.428	118.00%	34.3%	13	36
5.8		3	0.806	0.417	1.000	0.194	0.337	41.80%	80.0%	29	36
12		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36
21		3	1.000	1.000	1.000	0.000	0.000	0.00%	100.0%	36	36

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 03-5293-4723
Analyzed: 16 Jul-19 13:06Endpoint: Larval Mortality
Analysis: Linear Regression (GLM)CETIS Version: CETISv1.9.5
Status Level: 1

Graphics

Log-Normal: $\text{inv } \Phi[\pi] = \alpha + \beta \cdot \log[x]$ 

CETIS Analytical Report

Report Date: 21 Oct-19 21:07 (p 1 of 3)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 07-9434-0782 **Endpoint:** Adult Emergence Rate
Analyzed: 16 Jul-19 13:04 **Analysis:** Untrimmed Spearman-Kärber

CETIS Version: CETISv1.9.5
Status Level: 1

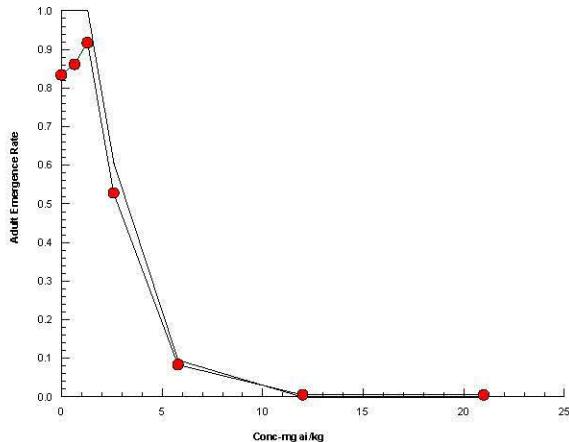
Batch ID: 17-1782-3927 **Test Type:** OECD 2014 HB Larval Repeat Exp
Start Date: 03 Oct-18 **Protocol:** Larval Chronic Oral Toxicity, 21-day Study
Ending Date: 20 Oct-18 **Species:** Apis mellifera
Test Length: 17d 0h **Taxon:**

Analyst:
Diluent:
Brine:
Source: Not Reported **Age:**

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	EC50	95% LCL	95% UCL
Control Threshold	0.167	0.00%	0.493	0.0311	3.11	2.7	3.59

Adult Emergence Rate Summary			Calculated Variate(A/B)					Isotonic Variate			
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.833	0.833	0.833	0.000	0.00%	0.0%	30/36	0.87	0.0%
0.66		3	0.861	0.833	0.917	0.048	5.59%	-3.33%	31/36	0.87	0.0%
1.3		3	0.917	0.833	1.000	0.083	9.09%	-10.0%	33/36	0.87	0.0%
2.6		3	0.528	0.167	0.750	0.315	59.80%	36.7%	19/36	0.528	39.4%
5.8		3	0.083	0.000	0.250	0.144	173.00%	90.0%	3/36	0.0833	90.4%
12		3	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%
21		3	0.000	0.000	0.000	0.000		100.0%	0/36	0	100.0%

Graphics

CETIS Analytical Report

Report Date: 21 Oct-19 21:07 (p 2 of 3)
 Test Code/ID: 50862201 dc / 16-2181-8188

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID: 08-4845-5116 **Endpoint:** Day 15 Mortality
Analyzed: 16 Jul-19 13:05 **Analysis:** Untrimmed Spearman-Kärber

CETIS Version: CETISv1.9.5
Status Level: 1

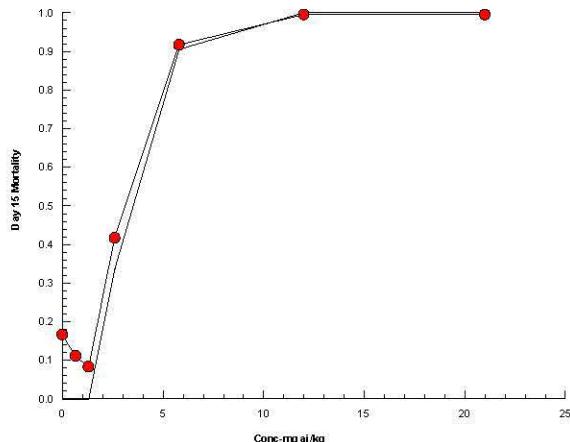
Batch ID: 17-1782-3927 **Test Type:** OECD 2014 HB Larval Repeat Exp
Start Date: 03 Oct-18 **Protocol:** Larval Chronic Oral Toxicity, 21-day Study
Ending Date: 20 Oct-18 **Species:** Apis mellifera
Test Length: 17d 0h **Taxon:**

Analyst:
Diluent:
Brine:
Source: Not Reported **Age:**

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.167	0.00%	0.511	0.0303	3.25	2.82	3.73

Day 15 Mortality Summary			Calculated Variate(A/B)					Isotonic Variate			
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.167	0.167	0.167	0.000	0.00%	0.0%	6/36	0.12	0.0%
0.66		3	0.111	0.083	0.167	0.048	43.30%	-6.67%	4/36	0.12	0.0%
1.3		3	0.083	0.000	0.167	0.083	100.00%	-10.0%	3/36	0.12	0.0%
2.6		3	0.417	0.167	0.833	0.363	87.20%	30.0%	15/36	0.417	33.7%
5.8		3	0.917	0.750	1.000	0.144	15.70%	90.0%	33/36	0.917	90.5%
12		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
21		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics

Special Study Honey bee Larval Chronic Oral Toxicity, 21-day Study

EAG, Inc.

Analysis ID:	20-6937-5380	Endpoint:	Larval Mortality	CETIS Version:	CETISv1.9.5
Analyzed:	16 Jul-19 13:06	Analysis:	Untrimmed Spearman-Kärber	Status Level:	1
Batch ID:	17-1782-3927	Test Type:	OECD 2014 HB Larval Repeat Exp	Analyst:	
Start Date:	03 Oct-18	Protocol:	Larval Chronic Oral Toxicity, 21-day Study	Diluent:	
Ending Date:	20 Oct-18	Species:	Apis mellifera	Brine:	
Test Length:	17d 0h	Taxon:		Source:	Not Reported
					Age:

Spearman-Kärber Estimates

Threshold Option	Threshold	Trim	Mu	Sigma	LC50	95% LCL	95% UCL
Control Threshold	0.0556	0.00%	0.547	0.0339	3.52	3.01	4.12

Larval Mortality Summary			Calculated Variate(A/B)						Isotonic Variate		
Conc-mg ai/kg	Code	Count	Mean	Min	Max	Std Dev	CV%	%Effect	A/B	Mean	%Effect
0	N	3	0.056	0.000	0.083	0.048	86.60%	0.0%	2/36	0.037	0.0%
0.66		3	0.028	0.000	0.083	0.048	173.00%	-2.94%	1/36	0.037	0.0%
1.3		3	0.028	0.000	0.083	0.048	173.00%	-2.94%	1/36	0.037	0.0%
2.6		3	0.361	0.000	0.833	0.428	118.00%	32.4%	13/36	0.361	33.7%
5.8		3	0.806	0.417	1.000	0.337	41.80%	79.4%	29/36	0.806	79.8%
12		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%
21		3	1.000	1.000	1.000	0.000	0.00%	100.0%	36/36	1	100.0%

Graphics

